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TITLE: Methods of using analogs of human basic fibroblast growth factor mutated at one or more of the positions glutamate 89, aspartate 101 or leucine 137

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INVENTOR-INFORMATION:

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CLAIMS:

What is claimed is:

1. A method of stimulating cell division which comprises: (A) contacting cells with an effective amount of one or more muteins of a human basic fibroblast growth factor, or biologically active peptides thereof in vitro, wherein said one or more muteins comprise the substitution of a neutral and/or hydrophobic amino acid for one or more of the following: (a) Glutamate 89; or (b) Aspartate 101; or (c) Leucine 137; wherein the numbering of amino acids is based on SEQ ID NO:1; or (B) contacting cells with an effective amount of said one or more muteins, or biologically active peptides thereof in vivo.

2. The method of claim 1, wherein said one or more muteins comprise the substitution of a hydrophobic amino acid for Glu.sup.89.

3. The method of claim 1, wherein said one or more muteins comprise the substitution of a hydrophobic amino acid for Asp.sup.101.

4. The method of claim 1, wherein said one or more muteins comprise the substitution of a hydrophobic amino acid for Leu.sup.137.

5. The method of claim 1, wherein said one or more muteins comprise the substitution of a neutral amino acid for Glu.sup.89.

6. The method of claim 1, wherein said one or more muteins comprise the substitution of a neutral amino acid for Asp.sup.101.

7. The method of claim 1, wherein said one or more muteins comprise the substitution of a neutral amino acid for Leu.sup.137.

8. The method of claim 1, wherein said neutral amino acid is defined as alanine and said hydrophobic amino acid is defined as tyrosine.

9. The method of claim 1, wherein said one or more muteins of human basic fibroblast growth factor, or biologically active peptides thereof, comprise one or more of the following substitutions: (a) substitution of Glutamate 89

with alanine or tyrosine; (b) substitution of Aspartate 101 with alanine; or (c) substitution of Leucine 137 with alanine; or any combination thereof, wherein the numbering of amino acids is based on SEQ ID NO:1.

10. The method of claim 9, wherein said mutein is human basic fibroblast growth factor [Ala.sup.89].

11. The method of claim 9, wherein said mutein is human basic fibroblast growth factor [Ala.sup.101].

12. The method of claim 9, wherein said mutein is human basic fibroblast growth factor [Ala.sup.137].

13. The method of claim 9, wherein said mutein is human basic fibroblast growth factor [Ala.sup.89, 101].

14. The method of claim 9, wherein said mutein is human basic fibroblast growth factor [Ala.sup.89, 137].

15. The method of claim 9, wherein said mutein is human basic fibroblast growth factor [Ala.sup.101, 137].

16. The method of claim 9, wherein said mutein is human basic fibroblast growth factor [Ala.sup.89, 101, 137].

17. The method of claim 9, wherein said mutein is human basic fibroblast growth factor [Tyr.sup.89].

18. The method of claim 1, wherein said mutein is a human basic fibroblast growth factor [Tyr.sup.137].

19. The method of claim 1, wherein said mutein is a human basic fibroblast growth factor [Tyr.sup.89, 101].

20. The method of claim 1, wherein said mutein is human basic fibroblast growth factor [Tyr.sup.89, 137].

21. The method of claim 1, wherein said mutein is human basic fibroblast growth factor [Tyr.sup.101, 137].

22. The method of claim 1, wherein said mutein is human basic fibroblast growth factor [Tyr.sup.89, 101, 137].

23. The method of claim 1, wherein said method comprises contacting cells in vivo.

24. The method of claim 1, wherein said effective amount in vitro is 0.001 picograms to 1000 micrograms per milliliter.

25. The method of claim 24, wherein said effective amount is 0.001 nanograms to 1000 nanograms per milliliter.

26. The method of claim 25, wherein said effective amount is 0.01 nanograms to 100 nanograms per milliliter.

27. The method of claim 1, wherein said effective amount in vivo is from about 0.001 pg/kg body weight to about 10 mg/kg body weight daily administered parenterally.

28. The method of claim 27, wherein said effective amount is from about 1 pg/kg body weight to 5 mg/kg body weight per day.

29. The method of claim 28, wherein said effective amount is from about 10 pg/kg body weight to about 1 mg/kg body weight daily.

30. The method of claim 1, wherein said neutral amino acid is selected from the group consisting of serine, threonine, alanine, asparagine, glutamine, cysteine, and glycine, and said hydrophobic amino acid is selected from the group consisting of tyrosine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine.